## REMARKS

In the Office Action, claims 1-5, 8, 9, 11-13, 15-17, 22, 23 and 49 are rejected under 35 U.S.C. §112, second paragraph. The Office correctly observes a portion of claim 1 had been inadvertently omitted in the previous paper, for which applicants apologize. The present Amendment obviates this rejection.

Claims 1-5, 8, 9, 11-13, 15-17, 22, 23, 37, 40, 41, 43, 44 and 46-51 are rejected under 35 U.S.C. §103 from Aoyama U.S. Patent No. 6,827,963 in view of Wester U.S. Patent No. 6,589,588, C.F.R. §101.83 and St.-Onge *et al.* "Consumption of a Functional Oil Rich in Phytosterols and Medium-Chain Triglyceride Oil Improves Plasma Profiles in Men," taken together, as further evidenced by Baileys and Pelloso U.S. Patent No. 5,434,278.

Each of independent claims 1, 37 and 40 is presently amended to specify that the medium chain triglyceride is a combination of caprylic triglyceride and capric triglyceride. These are, of course, of different carbon chain lengths, stated in the claims as a first fatty acid moiety chain and a second fatty acid moiety chain, respectively. The long chain domestic vegetable oil triglyceride is stated in the claims as having a third fatty acid moiety chain. One of ordinary skill in the art will understand that the first, second and third fatty acid moiety chains as presently claimed are different from each other.

The Office takes the position (for example, on page 6 of the Office Action), that Aoyama shows "all of the structural formulas possible from the random interesterification reaction of medium and long chain fatty acid sources with a source of glycerol." On page 10, the Office states that the "Examiner does not believe that the structural formulas of Aoyama and the claims are different."

As previously discussed, Aoyama posits a maximum of eight Formulas. These amount to two different variables in three different orderings, or $2^3$, which computes to the eight Formulas that Aoyama lists. However, applicants have three variables in three orderings, or $3^3$ possible chemical structures, calculating as 27 formulas randomly determined according to the claimed interesterification. Applicants respectively observe that the eight structural Formulas depicted in

Aoyama are different from the 27 randomly determined chemical structures according to the presently revised claims.

In addition, as previously observed, Aoyama does not truly disclose or teach that the Formulas listed by Aoyama are randomization products. The Office says randomization is taught by the simple statement "a chemical synthesis method" in column 8 of Aoyama. As previously discussed, Aoyama teaches away from a randomization product, even if all eight of the Aoyama Formulas could be made by any enabling or predictive disclosure of Aoyama.

Aoyama's enabling disclosure and teaching is esterification by the enzyme method. This enzyme method, according to the teaching of Aoyama itself at lines 34-38 of column 8, "**selectively makes reaction at the first and third portions of the triglyceride**." This teaches away from reaction at the second portion of the triglyceride. This teaches one of ordinary skill in the art away from a randomization reaction and product characteristic of applicants' claimed invention having interchanged moiety chains that vary randomly from glycerol structure to glycerol structure. Aoyama teaches away from randomness and correctly observes that the products of Aoyama are made selectively, favoring of reaction at only the first and third portions of the triglyceride.

Aoyama teaches driving its reaction toward a non-random array. For example, in Table I in column 9 of Aoyama, Aoyama Composition 1 has 84.7% Formula III or III', and Composition 2 has 38.4% Formula I and 31.4% of the same Formula III or III' of Composition 1.

These teachings of selective first and third site reactions and of having Compositions 1 and 2 drive toward a very few of the eight Formulas motivates one of ordinary skill in the art away from the randomization that applicants claim.

For at least these reasons, Aoyama does not disclose, teach or motivate one of ordinary skill in the art to arrive at applicants' claimed invention.

None of the secondary references remove these substantial and significant deficiencies of Aoyama. Applicants do not repeat in detail previous observations concerning these secondary references, other than the following summary observations. St.-Onge mentions **blends** of medium chain triglyceride

oil and phytosterols, without any suggestion that an MCT oil is to be interesterified with a long chain domestic oil. A blend is not an interesterification, and St.-Onge **teaches nothing about random interesterification as a means of enhancing phytosterol delivery**. Wester has no teaching concerning random interesterification or the liquid lipid components that are claimed presently. The Office relies on the C.F.R. reference and Bailey for showing certain properties without tying those in any way to random interesterified or phytosterol delivery enhancement.

Pelloso is cited as allegedly enabling in response to Aoyama's significant deficiencies in teaching anything about Aoyama's hollow words "chemical synthesis method." There is nothing in Pelloso to even remotely suggest or motivate one of ordinary skill in the art to combine a Pelloso product with a phytosterol and expect that the Pelloso product would enhance delivery of the phytosterol.

In the paragraph common to pages 13 and 14 of the Office Action, the Office seeks to respond to applicants' prior refutation of the *prima facie* obviousness position taken by the Office. Particularly pointed is the statement in the Office Action that the subjects tested in St.-Onge were different from the subjects tested in Rudkowska "in that the Rudkowska subjects were hyperlipidemic at the start of the testing." The Office in effect says that the comparison is not valid because the recognized enhancement in LDL cholesterol reduction is merely expected as one would expect hyperlipidemic subjects to experience a bigger change in diet. Closer examination indicates that this is more in the nature of a semantic difference.

In the top of the first column of page 2 of St.-Onge, the subjects of the study were identified as having a TC (total cholesterol) concentration below 7.0 mmol/L and a TG (triglycerides) of below 3.0 mmol/L, also stating that the subjects had no history of "diabetes, hypothyroidism, hypertension or other known metabolic disorders and had a body mass index between 25 and 31 $kg/M^2$." The clinical study noted in Rudkowska is disclosed in greater detail in applicants' co-pending Application No. 10/598,215, a continuation-in-part of the

subject application, and which is Publication No. 2007/0141221. Table IV in paragraph [0111] of the '221 publication shows that the average TC of the subjects of applicants' clinical study was 5.90 mmol/L (which is below 7.0 mmol/L). Table IV also discloses that the TG average was 1.92 mmol/L (which is below 3.0 mmol/L). This is consistent with page 392 of Rudkowska itself, disclosing an LDL-C of more than 3 mmol/L. That same paragraph of Rudkowska states that the subjects were excluded if they had "diabetes, hypertension, hypothyroidism or other known metabolic disorders."

Despite these remarkable similarities between the respective subjects of the two clinical studies, the effects were markedly different. The effect of the St.-Onge delivery of phytosterol by blends is relatively low compared with applicants' claimed delivery of phytosterols by the random interesterified products. Applicants' clinical study conclusively reports an **enhanced reduction of half again** the enhancement reported by St.-Onge.

Applicants note with understanding the Examiner's observation at the top of page 14 of the Office Action that the Rudkowska test was not designed to compare applicants' invention with that of the combination of references presented in the Office Action. A clinical study is not the same as an inexpensive lab test, but represents large investments in time, money and care for the human subjects. Applicants should not be held to a standard that would require applicants to rerun such a human study because applicants could not anticipate the Office's present combination of references. That said, it is hard to imagine how the clinical test run by applicants could have been much closer to the combination of references presented by the Office, even if it were possible to have designed it precisely for this purpose.

After all, besides the remarkable similarities in the respective subjects pointed out above, the 2006 Rudkowska publication (applicants' claimed composition and methods) and the 2003 St.-Onge prior art relied upon by the Office each report on clinical testing of men having a body mass index of 25-31 $kg/m^2$. Twenty-three of these men completed the study using applicants' invention, while thirty men were in the study of the 2003 St.-Onge publication.

Each study followed a randomized crossover type of test, and each delivered the phytosterol-containing component with the same isoenergetic meal protocol of 15% protein, 40% fat and 45% carbohydrates. In the 2006 clinical study according to applicants' claimed invention, blood samples were taken at days 1, 2, 41 and 42, whereas in the 2003 St.-Onge clinical study, blood samples were taken at days 1, 28 and 29. Each analyzed the blood samples and calculated LDL cholesterol using the Friedenwald formula.

The baseline LDL for applicants' invention was 3.59, same being reduced to the end point value of 3.12, **a reduction of 21%**. *See* data in the table on page 393 in the "Functional Oil" columns and the "LDL-C" rows. As reported in Table 3 on page 1817 of the St.-Onge publication, the baseline for the functional oil (FctO) for LDL-C was 3.43, and the Endpoint was 2.96, **a reduction of 14%**. Thus, **there is a 7% greater baseline reduction with applicants' invention when compared with St.-Onge**. This is an enhancement of **half again the enhancement** reported for St. Onge.

The combination of references does not provide significant predictability of this magnitude of enhanced effectiveness when the randomization interesterification products of the present claims are combined with phytosterols. The art provides no predictability that the randomly interesterified lipids would deliver the phytosterols with the enhanced effectiveness evident by these data.

Accordingly, these data provide further strong support for the unobviousness of the presently claimed invention. Reconsideration and withdrawal of the §103 rejection is believed to be in order for this additional reason.

Applicants have made an earnest endeavor to place this application into condition for allowance, and favorable consideration is respectfully requested.

Respectfully submitted

/Raymond M. Mehler/
Raymond M. Mehler
Registration No.: 26,306

COOK ALEX LTD.
200 West Adams Street
Suite 2850
Chicago, Illinois 60606
(312) 236-8500

Dated: June 23, 2011